



NOTES

ADRENAL HYPOFUNCTION

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Disorders of adrenal cortex resulting in loss of essential steroid hormones (corticosteroids, mineralocorticoids, androgens)

CAUSES

- Addison's disease
 - Multiple causes; primarily autoimmune
- Waterhouse–Friderichsen syndrome (WFS)
 - Primarily caused by meningococcal infection, sepsis

COMPLICATIONS

- Adrenal crisis
 - Addison's, WFS
- Disseminated intravascular coagulation
 - WFS

SIGNS & SYMPTOMS

- Hypoglycemia, hypotension, electrolyte imbalance
- Adrenal crisis:** dehydration, electrolyte imbalance, shock

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound, CT scan

- Visualizes enlarged, calcified, solid/hemorrhagic glands

OTHER DIAGNOSTICS

- Rapid adrenocorticotrophic hormone (ACTH) test confirms adrenal hypofunction

TREATMENT

MEDICATIONS

- Hormone replacement:** hydrocortisone, fludrocortisone
 - Dehydroepiandrosterone (DHEA) in some cases

OTHER INTERVENTIONS

- Treat underlying cause

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ADDISON'S DISEASE

osms.it/addisons-disease

PATHOLOGY & CAUSES

- Endocrine disorder characterized by **primary adrenal insufficiency** due to bilateral adrenal cortex destruction
- Adrenal cortex destruction → ↓ production of adrenocortical hormones → **glucocorticoid, mineralocorticoid, androgen deficiency**
 - Adrenals only source of androgens in biologically-female individuals; testes supply androgens in biologically-male individuals
- ↓ **cortisol** → ↓ adrenal medullary epinephrine synthesis → ↓ serum epinephrine, compensatory norepinephrine production

CAUSES

- **Autoimmune destruction** (e.g. polyglandular autoimmune syndrome type 2)
- **Infection** (e.g. tuberculosis, fungal infections)
- Adrenal hemorrhage (e.g. WFS)
- Adrenal vein thrombotic infarction
- Metastatic infiltration
- Drugs that inhibit cortisol biosynthesis (e.g. ketoconazole, suramin)

COMPLICATIONS

- Addisonian crisis precipitated by physiologically stressful events (e.g. surgical procedures, trauma, infection, dehydration)

SIGNS & SYMPTOMS

- Fatigue, weakness are common initial symptoms
- **Hypotension**, postural hypotension, syncope
 - ↓ glucocorticoids → ↓ vascular responsiveness to angiotensin II and

norepinephrine

- **Hyponatremia**
 - Mineralocorticoid deficiency → sodium loss + ↓ **volume** due to ↑ vasopressin secretion secondary to ↓ cortisol
- **Hyperkalemia**, mild hyperchloremic acidosis due to mineralocorticoid deficiency
- Hypoglycemia due to ↓ gluconeogenesis
- Gastrointestinal
 - Abdominal pain, anorexia, nausea, vomiting → weight loss
- Intolerance of temperature extremes
- **Hyperpigmentation** due to **ACTH stimulation of melanocyte activity**
- Vitiligo due to autoimmune destruction of melanocytes
- Salt cravings due to hyponatremia
- ↓ libido, ↓ pubic, axillary hair in biologically-female individuals due to ↓ adrenal androgens
- Psychiatric symptoms (e.g. confusion, depression)
- Addisonian crisis triggered by stress
 - Hypoglycemia
 - Vasomotor/circulatory collapse; shock may be unresponsive to vasopressors due to ↓↓ cortisol, potentially fatal



Figure 13.1 An example of increased skin pigmentation in an individual with Addison's disease (left) and resolution post-treatment (right).



Figure 13.2 Hyperpigmentation of the gums in an individual with Addison's disease.

- ↑ serum ACTH
- Plasma renin activity
 - ↑ renin, compensatory to ↓ aldosterone
- ↓ serum sodium, ↑ serum potassium, mild hyperchloremic acidosis

OTHER DIAGNOSTICS

- History, physical examination with characteristic findings
- Rapid ACTH test
 - Administer 250µg synthetic ACTH (cosyntropin) intravenous (IV)/intramuscular (IM) → insufficient/no cortisol produced in response

DIAGNOSIS

DIAGNOSTIC IMAGING

Abdominal CT scan

- Enlarged adrenal glands with tuberculosis/malignant mass; small if autoimmune adrenalitis/advanced tuberculosis; calcifications if infectious cause
- Visualizes adrenal gland hemorrhage/thrombosis

Abdominal X-ray

- Adrenal calcifications if infectious cause

LAB RESULTS

- ↓ serum cortisol
 - Blood draw in AM when cortisol levels should peak

TREATMENT

MEDICATIONS

- Life-long glucocorticoid replacement; e.g. hydrocortisone, mineralocorticoid replacement
 - E.g. fludrocortisone
- Biologically-female individuals may need low dose dehydroepiandrosterone (DHEA)
- Addisonian crisis
 - Glucocorticoids, epinephrine, glucose, isotonic fluids
- Stress dose of glucocorticoid during any surgical intervention/significant trauma
 - Premedication/induction-maintenance-gradual titration to baseline dose

WATERHOUSE-FRIDERICHSEN SYNDROME

osms.it/waterhouse-friderichsen

PATHOLOGY & CAUSES

- Uncommon, severe syndrome characterized by adrenal failure related to overwhelming infection, adrenal gland hemorrhage

- Bacterial infection → septicemia → release of bacterial endotoxins → endothelial dysfunction → seeding of bacterial emboli into adrenals → bleeding into one/both

adrenal glands → hemorrhagic necrosis → adrenocortical insufficiency → adrenal crisis

CAUSES

- Associated with sepsis caused by organisms (e.g. *Neisseria meningitidis* (80% of cases), *Streptococcus pneumoniae*, *Neisseria gonorrhoeae*, *Escherichia coli*, *Haemophilus influenzae*, *Staphylococcus aureus*)

COMPLICATIONS

- Disseminated intravascular coagulation (DIC)
- Profound shock
- Potentially life-threatening

SIGNS & SYMPTOMS

- **Initial presentation:** malaise, fever, chills, headache, vomiting
- Signs of shock (e.g. hypotension, tachycardia, tachypnea)
- Widespread petechial lesions → purpura → plaques
- Cyanosis, AKA dusky gray color of skin

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Identifies blood collection within adrenals

Ultrasound

- Adrenal hemorrhage appears solid, diffusely echogenic

LAB RESULTS

- Blood culture
 - Identifies causative organism
- Adrenal insufficiency
 - ↓ serum sodium, ↓ glucose, ↑ potassium, ↓ serum cortisol
- DIC
 - ↑ fibrinogen degradation products, ↑ D-dimer levels, prolonged PT, aPTT

OTHER DIAGNOSTICS

- History, physical examination with characteristic findings
- Rapid ACTH test
 - Insufficient/no cortisol produced indicates adrenal insufficiency

TREATMENT

MEDICATIONS

- Adrenal insufficiency
 - IV glucocorticoids
- Infection
 - Antibiotics (e.g. IV penicillin, cefotaxime/ceftriaxone if meningococcal infection)
- Shock
 - IV fluids, vasopressors, supplemental oxygen
- DIC
 - Packed red blood cells (RBCs), cryoprecipitate, fresh frozen plasma, platelets

OTHER INTERVENTIONS

- Prevention
 - Routine vaccination against meningococcal disease